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Volume XXIV Toronto, November, 1946 Number 2

The University of Toronto Medical Journal

(AN UNDERGRADUATE PUBLICATION)

This journal is published six times a year, November to April, by the Medical Society of the University of Toronto, to serve as a medium for student expression and to bring to the student recent articles of scientific interest.

$1.50 per volume. 25c. per single copy.

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CAUSATION IN PATHOLOGY

By T. D. MUIR, B.A.

I use "pathology" in this broad sense: the science of disease. But there need not be disagreement with the specialist over area of application, for I believe that the following thesis is generally applicable. Simply it is: The cause of disease is not merely some single factor. It is a more or less complex of factors—that complex consisting of a nucleus or core factor with secondary factors of more or less importance electron-like about it.

Generally that core factor is a germ. To the functionalist I would reply that HIS core factor, though not an entity like the tubercle bacillus, nevertheless is the for-the-time-being central factor, whether vitamin deficiency or hypothyroidism. I have used "for-the-time-being" to cover the possibility that at base there IS a germ; nevertheless I believe that whatever the disagreement as to the actual core factor our thesis holds true.

Now then—to be specific—are we arguing that the cause of tuberculosis for example is not merely the tubercle bacillus? Yes. And the critical word is "merely". For though it may be argued that John Brown would not have had tuberculosis if tubercle bacilli had never existed, it cannot be argued that because

they existed, then he or anyone else would have had that disease. Our first statement indicates the essentiality of the tubercle bacillus to the causing of tuberculosis. The second indicates its insufficiency. For until tubercle bacilli locate in the human organism under favourable conditions the casual complex is incomplete. Tuberculosis does not follow.

This seems so simple, so obvious, that the stating may incur the comment "Trite!". Yet it is a necessary step in our analysis, which now indicates that as we move from the Caused to the Causing, as we examine not only the nature of the tubercle bacillus but also the significance of "locate in" and "under favourable conditions", then the causal picture expands. It is seen to be what we named it —complex; and the persistent investigator finds that it involves Sociology as well as Biology, Politics as well as Chemistry, Philosophy as well as Physics. Sociology, for the science of human groups bears on Tuberculosis. Politics, for the science of government bears thereon. Philosophy, for the study of all knowledge bears thereon.

He who cannot see, for example, a causal relation between the Nietzschean Will-to-Power philosophy and the present appalling Polish tuberculosis rate simply has not looked closely enough. Easier to see are the preventative value of a law requiring regular chest X-raying, and the fact that increased tuberculosis follows the group conflict war. But of course we are not arguing that "The Will to Power" eventually will raise the tuberculosis rate in Poland or that avoidance of such philosophy will mean the prevention of tuberculosis in Poland or elsewhere. We do not mean that the mere passing of a law will eradicate the disease, or that war eradicated means tuberculosis eradicated. But the passing of laws, the resolution of social conflicts, the eradication of selfish I'm-the-King-of-the-Castle philosophies can help destroy tuberculosis or any other disease. In other words such "non-organic" extraneous factors can be, indeed ARE part of the causal complex which brings about disease. Perhaps there are some readers who see nothing relevant between Nietzschean philosophy and the present frequency of tuberculosis in Poland. It would be useless to argue with them if they will not concede any connection between German aggression involving Poland and the influence on the Nazi hierarchy exerted by Nietzschean and similar radical power ideas.

Naturally we should be careful not to overestimate the "idea" factor, yet we may fairly argue that if Hitler, Goëring et al had believed quite differently—had really believed in, let us say, the golden rule—then the Polish tuberculosis rate would not be so high. We would remind our readers that the causal value of such factors has too often been neglected. Indeed, the encouraging growth of psychosomatic medicine now reflects recognition of that neglect and a real effort to do something about it. Further, it would be wrong to conclude that such secondary factors are of concern only in the problem of so-called functional disorders. We maintain, rephrased, our initial point: that all disease (organic or functional) is caused by a complex of factors.

Specifically, we do not imply that a hopeful, cheerful mental state will cure tuberculosis. We do imply that hope and cheer can help. It is not argued that a dejected and dreary mental state will cause tuberculosis. It is argued that that can help cause it. What is this all but simply recognition of the fact that generally our notion of causation in pathology has been too narrow?

We do not propose to assess here the relative importance of secondary factors to the core factor, whether it be the tubercle bacillus or the gonococcus, cell aberration or vitamin deficiency. Sufficient to stress that disease follows from a causal complex, not simply from a single cause; and if the ultimate goal of pathology is the eradication of disease, then the most effective strategy would be to attack all that complex, not merely its central factor. And to do this, the medical man will eventually find—if he has not already found—that he needs the help of the mathematician, the sociologist, the astronomer, the philosopher, the farmer, the fisherman, the minister, even the street-cleaner and the garbage-man as well as the psychologist, and chemist, and engineer in the common battle against disease. Needs, as they indeed need him.

The doctor's role in that battle is both tragic and triumphant. Tragic, in that too often he is called into the struggle late, after the causative factors have combined to initiate their attack and gain their ground; and yet triumphant so often in spite of this strategic handicap because he may help to turn the tide against the foe. For the humble one, that tragedy is softened that triumph is rendered not too personal by realizing his own relative causal function in the scheme of things. Life teaches him—sometimes by hard experience—that this literally IS a Uni-verse, in spite of its at times baffling complexities, one vast Ever-Becoming Whole. And so, because of this, the explanation of disease lies in part—yes, probably in more part than he would once have cared to concede—beyond the field of his doctorial vision. Yet, attainable? Yes. Improved technique and improved instruments (microscope, serum, or drug) will enlarge knowledge, we know. These are not neglected; but often this means is: Changing the mental perspective—trying to see a problem from the standpoint of a chemist, psychiatrist, farmer, or legislator. True, one cannot acquire the varied special experience which gives each of these his own particular viewpoint, but one may enlarge one's own field of vision by seeing through their eyes so to speak.

And so, concluding, thus might we spur on the seasoned searcher after cancer's cause as well as the freshman uncertain of to-morrow's testing: Do not be finally discouraged in the Fight. Remember the simple wisdom of your old schooltime fable—

THE BLIND MEN AND THE ELEPHANT

It was six men of Indostan,
To learning much inclined,
Who went to see the elephant,
(Though all of them were blind),
That each by observation
Might satisfy his mind.

The first approached the elephant
And, happening to fall
Against his broad and sturdy side,
At once began to bawl:
"Why, bless me! but the elephant
Is very like a wall!"

The second, feeling of the tusk,
Cried: "Ho! what have we here
So very round and smooth and sharp?
To me, 'tis very clear,
This wonder of an elephant
Is very like a spear!"

The third approached the animal
And, happening to take
The squirming trunk within his hands,
Thus boldly up he spake:
"I see," quoth he, "the elephant
Is very like a snake!"

The fourth reached out his eager hand
And felt about the knee:
"What most this wondrous beast is like
Is very plain," quoth he:
"'Tis clear enough the elephant
Is very like a tree!"

The fifth who chanced to touch the ear,
Said: "E'en the blindest man
Can tell what this resembles most—
Deny the fact who can:
This marvel of an elephant
Is very like a fan!"

The sixth no sooner had begun
About the beast to grope
Than, seizing on the swinging tail
That fell within his scope,
"I see," quoth he, "the elephant
Is very like a rope!"

And so these men of Indostan
Disputed, loud and long,
Each in his own opinion
Exceeding stiff and strong;
Though each was partly in the right,
And all were in the wrong.

(J. G. Saxe)

Kingston, Ontario, November 4th, 1946

T. D. Muir

TO THOSE STUDENTS OF ANATOMY WHO HAVE SMALL LATIN AND LESS GREEK

By J. C. B. GRANT, M.B., F.R.C.S. (Edin.)
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To those students of Anatomy who have "small Latin, and less Greek," consolation and courage, for in this respect you rank with William Shakespeare. Nor is it too late to achieve much regarding this shortcoming in your education, and Anatomy may hold the door; at least, it will allow you, by a reversal of the usual school procedure, to acquire a Latin and Greek vocabulary through anatomical terms and thereby to enhance your appreciation of the English language. Need it be said that it is not with a view to affording a vocabulary of anatomical and medical terms that courses in the classical languages are offered in our schools.

Our anatomical tradition takes us back beyond to the Greeks, back to the third century B.C., back to Alexandria on the delta of the Nile founded by and called after Alexander the Great, Aristotle's royal pupil. To Aristotle we owe the word *enteron* for intestine; from it are derived words such as meso-enteron or mesentery, dysentery, and enteric (or typhoid) fever. To an anatomist at Alexandria we owe the word *duodenum* for the first part of the enteron. This he observed to be as long as twelve fingers are broad, hence in Greek he called it the do-deka-daktulos (2-10-fingers), later to be corrupted into duodenum, duo-decim being Latin for 2-10, that is, for twelve. Evidently, then, to decimate is not to annihilate or exterminate, as certain newspaper reporters would have us think, but to destroy one in every ten.

Twelve islands, of which Rhodes is the largest, lie at the eastern end of the Mediterranean and are known as the Dodecanese Islands, but if you prefer to call them the Duodenal Islands, there is precedent to support you. The island of Rhodes means the island of roses. Rhododendron is Greek for a rose tree, dendron being a tree. Hence, the dendron or *dendrite* of a nerve cell is a process having the appearance of a tree, and the appearance of a dendrite ulcer of the cornea can readily be imagined.

Diminutive Terms. The Fascists of Italy have appropriated as their badge the fasces which was the emblem of authority in ancient Rome. This was an axe embedded in a bundle of rods of elm or birch, tied securely together, and having the obvious and forceful significance that the people (the rods or branches) were subject to authority (the axe). Fascis is Latin for a bundle. The diminutive term, *fasciculus,* is Latin for a small bundle and it is commonly applied to a small bundle of fibres, particularly of nerves and muscles. The Latin terminations—ulus,—ula, —ulum, which in English become—le, are frequently recurring in anatomical writings and suggest things diminutive or small. Even the advertisements in the daily papers refer to the *cuticle* (Latin cutis = skin) or film of skin which, unless restrained, spreads over the *lunule* (L. luna = moon) or small moon near the root of the finger-nail. The *clavicle,* which is the first bone you encountered, is probably so-called from its resemblance to the piece of stick used in olden days as a key to raise the

Reprinted from Volume XVIII No. 6 of the University of Toronto Medical Journal.

primitive latch of a door (L. clavis = a key; clavicula = a small key). The word for a blood cell or blood *corpuscle* is derived from Latin corpus = a body; corpusculus = a small body; and the words corpse for a dead body and corps, as in O.T.C., have the same derivation. A *glomerulus* of the kidney resembles a small ball (L. glomus = a ball). The word *tubercle* (L. tuber = a swelling; dim. tuberculum) is another such word; a potato is a tuber; a small swelling on a bone is a tubercle; and in the pathological condition known as tuberculosis small round inflammatory swellings, called tubercles, are scattered through the lungs and other organs. The chambers of the heart, *auricle* and *ventricle,* are diminutive terms (L. auris = ear; dim. auricula. L. venter = belly or stomach; dim. ventriculus). Other such words are: capsa = a box, dim. capsula = a *capsule;* lobus = a lobe, dim. lobulus = a *lobule;* malleus = a hammer, dim. *malleolus;* navis = a ship, dim. adjective *navicular,* hence the navy and the navicular bone.

Doubtless, you could extend this list; you could add the word *muscle* (L. mus = a mouse; musculus = a little mouse) meaning a small male mouse, because it would be muscula if it were a female mouse, and musculum if it were neuter. Hence the names of all muscles are masculine, e.g., musculus trapezius, musculus deltoideus, musculus gluteus maximus, musculus rectus abdominis or straight muscle of the abdomen, and musculus pectoralis major (minor) or the larger (smaller) muscle of the chest—had it been neuter it would be majus (Minus). For the sake of brevity, however, it is customary to omit the noun(musculus) while retaining the qualifying adjective (e.g., trapezius, deltoideus, rectus, biceps).

Tunica (Latin for a tunic or coat) is an example of a feminine word commonly omitted, e.g., Tunica cornea = the horny coat; T. sclera = the tough coat; T. conjunctiva = the conjoined or united coat; T. media = the middle coat; T. submucosa = the submucous coat.

Intestinum (Latin for the bowel or guts) is a neuter word commonly omitted, e.g., intestinum duodenum (discussed above); i. jejunum = the empty intestine; i. ileum = the twisted intestine; i. rectum = the straight intestine. The rectum takes the shape of the sacrum and, therefore, is straight in lower animals, but in man who walks erect the sacrum is curved and so is the rectum.

Suffixes. Forma is Latin and *Eidos* is Greek for shaped-like or resembling, and they are employed as suffixes thus:—form and—oid. Examples are cribriform = like a sieve; cuneiform = like a wedge; falciform = like a sickle; lentiform = like a lentil or lens; piriform = like a pear; pisiform = like a pea; sacciform =like a sac or bag; and vermiform = like a worm. Clinoid = like a bed, hence clinical medicine and clinics; conoid =like a cone; coracoid =like a crow (crow's beak); cricoid = like a ring; cuboid = like a cube; ethmoid = like a sieve; hyoid = U-oid or like the letter U; mastoid = like a breast; sigmoid = like the letter sigma or S; sphenoid = like a wedge; thyroid = like a shield; trapezoid = like the trapezium; typhoid fever =like typhus fever; and tabloid =like a tablet, and is a proprietary name for the tablets of a certain English Chemical Firm.

A few recurring Root Words. Akros (Gk.) = a point or summit; e.g., acromion (akros & omos = point and shoulder), acromegaly, acrocephaly, acropolis,

acrobat. *Didumos* (Gk. = a twin, hence the testis; e.g., epididymis = the organ "on the testis" and paradidymis = the organ "beside the testis" *Ducere* (ductum L.) = to lead; e.g., abduct (ab = from); adduct (ad = to); aqueduct (aqua = water); Il duce = the leader. *Fornix* (Gk.) = an arch, e.g., of the conjunctiva, vagina, and brain. *Genesis* (Gk.) = the first book in the Bible = beginning, origin, creation; c.f., gene, genetics, eugenics, genital generation. *Lemma* (Gk.) = a husk; e.g., neurilemma, sarcolemma (sarx = flesh, hence sarcomere, sarcoma, sarcophagus). *Phusis* (Gk.) = growth; e.g., diaphysis or the part growing between the two ends of a bone; symphysis or growth together, as in symphysis pubis and symphysis menti; epiphysis or growth upon; and hypophysis cerebri or growth under the brain, also called the pituitary gland. *Skopein* (Gk.) = to look at or examine; e.g., microscope (mikros = small); laryngoscope; ophthalmoscope; periscope (peri = around); stethscope (stethos = the chest); and telescope (tele = at a distance, far off).

Prefixes. Circum is Latin and *peri* is Greek for round about, around. Circumference is Latin for periphery, which is Greek. Examples: circumduct (lead or conduct around), circumflex (bend around), circumvallate (rampart around), and circumcise (cut around). Pericardium (around the heart), perichondrium (around cartilage), periosteum (around bone), perineal (around the "anus and urethra"), and peritoneum (stretched around), and periscope (look around).

Dia (Gk. = between, through, across; e.g., diaphragm = a partition between; diameter = a measurement across; diarrhoea = to flow through; *diabetes* = to pass through or syphon. and di(a)encephalon = the in-between-brain.

Epi (Gk.) = upon; e.g., epidermis = "upon the skin"; *epiphysis* = growth upon; *epiglottis; epitympanum;* and *epidemic* (demos = the people—hence democracy) = a disease descending on the people.

Hypo (Gk.) and *Sub* (L.) = under, below; hence hypodermic and subcutaneous, dermis being Greek for skin, and cutis being Latin.

Hyper (Gk.) and *Supra* (L.) = above, over, excessive; hence hypernephric and suprarenal, nephros being Greek for kidney, and ren being Latin.

Para (Gk.) = beside, alongside; e.g., paracolic fossa, paranasal sinuses, parathyroid gland, paradidymis, paraovarium, parotid (ous, otikos = the ear) gland, and parallel lines.

Pro (L. and Gk.) = before; e.g., prostate = the gland standing before the bladder; pronephros = the front (cervical) kidney; projection = thrown forwards; protuberance = a forward tuber or swelling; protract = to pull forwards; and prognosis = known beforehand.

Meta (Gk.) = beyond, after, over; e.g., metacarpals and metatarsals = the bones beyond the carpals and tarsals; metopic = beyond the optic or eye region; metanephros = the after or hind kidney; and metabolism and metaphor.

Syn (Gk.) = with, together with; e.g., synchondrosis = united with cartilage; synbiosis (bios = life; hence biology) = living together; synchronise = timed together (chronos = time, ch., chronic); synapse = joined together (aptein = to

join); synopsis (opsis = a view) = a general view; symposium (potes = a drinker) = a drinking party; and synagogue.

Tele (Gk.); distant, end; e.g., telencephalon = the end brain; telescope (skopein = to see); telephone (phone = the voice); and teleology.

Trans (L.) = across, through; e.g,. transpyloric plane; transfuse (fusus = poured); transverse (versus = turned) = turned across the long axis; translucent (lucere = to shine); transparent (parer = to appear); transpire (spirare = to breathe) and transude (sudare = to sweat).

A v. A: A in Greek = not, the negative; e.g., aseptic (septos = decay) means not-decayed; and atrophic (trophe = nourishment) means not-nourished. A or Ab in Latin = from, away from; e.g., to avert (vertere = to turn) means to turn away from; and to abduct (ducere = to lead) means to lead away from. Non is Latin for not, the negative; e.g., non-vascular vas = a vessel; vasculum = a small vessel), vas being a Latin word, avascular would mean "from vascular".

Dis v. Dys: Dis (L.) apart, asunder; e.g., dissect (secare = to cut) = to cut apart; dislocate (locare = to place) = to put out of place; and disseminate (seminare = to sow; semen = seed) = to scatter seed. Dys (Gk.) = difficult, painful, not good; e.g., dyspepsia (pepsis = digestion); dystrophy trophe = nourishment; c.f., atrophy, hypertrophy); and dysentery (enteron = intestine).

Ante v. Anti: Ante (L.) =before, in front of; e.g., anterior, anteflexed, antebrachial, ante-"room", and ante-"dated". Anti (Gk.) = opposite, against; e.g., antihelix, antitoxin, antidote, and antagonist.

Coli v. Colli: Coli (L.) = of the colon. Colli (L.) = of the neck.

Ileum v. Ilium (L.) are neuter adjectives. Intestinum ileum = the twisted intestine; os ilium = the flank bone.

Inter v. Intra (L.) are prepositions. Inter = between; intra = inside, within; e.g., interlobular = between lobes; intralobular = inside lobes.

Os v. Os: Os (oris, L.) masculine = a mouth. Os (ossis, L.) neuter = a bone.

Perineal v. Peroneal are (Gk.) adjectives. Perineal = around the "anus and urethra". Peroneal = fibular; perone being a fibula or a pin.

Of all anatomical terms, certainly of all anatomical eponyms, you would imagine *tendo Achillis* to be the most ancient, dating back to Homeric days and the seige of Troy, but Dr. J. Harold Couch, in a short paper published in the Canadian Medical Journal, page 668, June, 1936, dispells this notion and attributes the term to Philip Verheyen, Professor of Anatomy in the University of Louvain, who introduced it into our nomenclature in 1693, as *Chorda Achillis,* later to be modified to tendo Achillis, and now commonly called the *tendo calcaneus.* Indeed, with the advance of knowledge, it becomes necessary to make and to introduce new names, hence most anatomical terms are post-renaissance words.

If you have doubt as to the correctness of the interpretation given here to any word, your appeal is to the dictionary—to a Latin and a Greek dictionary, the Shorter Oxford English Dictionary, and a medical dictionary; and their value diminishes in this order.

Feature

C. L. RODGERS, Editor

BATTLE OF FURUNCULUS

(A lay made about the year Twenty-one of the Constitution.)

Staphylococcus Aureus,
By Gram and Koch he swore
He would invade new regions
Unconquered heretofore,
By Gram and Koch he swore it—
To take a patient's life
And called the Cocci, young and old,
From all the colonies of gold
To aid him in the strife.

Loud rang the warning toxins,
And flashed the summons forth
On the distant slopes of Agar
And the turbid seas of Broth;
The Cocci clustered thickly
From far off lands and labs.
Cocci of ancient culture came,
To come by tube they thought no shame,
But others of a fiercer fame
Drove up in acne scabs.

The septic hosts of Cocci
Advanced in serried ranks,
They marched upon the Blood Stream,
And camped upon its banks;
Forth flew the watchful blood-cells
Crying in wild turmoil:
"Staphylococcus Aureus
Has come and raised a boil;"
Far down the purple current
Was borne the direful shout—
The polymorphonuclears
And lymphocytes rush out;
Shame on the Eosinophile,
Who comes not forth to foil
The deadly Golden Coccus
At the Battle of the Boil!

And fiercely raged the conflict,
And thick lay strewn the dead:
The Battle of Furunculus
Was coming to a head!
The pale and lifeless pus cells
In scores were borne away,
But not a single Coccus
Survived that bloody fray.

Staphylococcus Aureus
Still wields his golden chain,
Where falling in the central slough
His friends around lie slain;
Surrounded and outnumbered
Still valiantly he fights—
He sees his tawny hosts grow less,
He sees the battle's hopelessness
Yet ever through the Yellow Press
Defies the leucocytes.

Staphylococcus Aureus
Has fallen in the fray,
Upon a martial coverslip
They bore his corpse away—
Lying in state in Canada
Embalmed he long remained
For though he dyed Gram positive
His honour was unstained.

And still at festive seasons,
When the blood is really stirred,
Before the full post-prandial rise
Of white cells has occurred,
When the phagocytes sit waiting
With platelets undersized
For the evening meal of microbes
Which is being opsinized;

When the trembling Eosinophyle
That wrought the deed of shame,
Immune from fresh invasion
Comes forth his share to claim,
And talks of Staphylococcus,
And mocks his ancient frame
(For now the Yellow Peril
Is nothing but a name).

Some old and hoary leucocyte,
Who finds he's in the vein,
Will tell the well-known story
Of his battles once again;
While blood cells sit in rouleaux round
To hear the tale retold
Of the Battle of Furunculus
In the brave days of old.

Reprinted from "Round the Fountain" and St. Bart's Hospital Journal.
R.B.P., S.B.H.J., Oct. 1909.

THE PHARMACOLOGY OF DIGITALIS

J. K. W. FERGUSON, Professor of Pharmacy and Pharmacology

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The most important active constituent of powdered Digitalis is probably a glycoside, now well known as Digitoxin. Many other glycosides can be extracted from the powdered leaf and some of these have actions more or less similar to those of Digitoxin. Others again are known as saponins and have irritant and hæmolytic properties but not the effects on cardiac muscle which distinguish the group of cardiac glycosides. Hundreds of papers have been published describing the various actions of Digitalis as exerted by one or more of scores of different preparations of varying degrees of purity. The actions of impure preparations are, of course, of practical interest but we have come to the stage where we can advance our understanding of these important drugs only by focusing on the measurable effects of highly purified preparations.

Two such preparations, which are now easily available, are Digitoxin and Digoxin. Others less well known are the Lanatosides A, B and C. All but Digitoxin are obtained from Digitalis lanata, rather than from the officially recognized species, Digitalis purpurea.

All of these glycosides share a common action from which they derive their group name of cardiac glycosides. When sufficient doses are injected into frogs to kill them, the ventricle of the heart is found to be contracted, pale and bloodless, a state described as "systolic arrest". All of these glycosides have also the property of relieving the symptoms of congestive heart failure in humans. Cardiac glycosides are found not only in the different species of Digitalis but in many other plants such as Strophanthus, Squill and Lily of the Valley.

The relief of congestive heart failure is often accompanied by a dramatic diuresis, which was noticed first by William Withering in 1775 (1). After ten years of careful trial and observation on his patients, he published a book in which he formulated excellent practical rules for the use of the drug in the treatment of dropsies. In Withering's time the relation between cardiac failure and œdema was not known, and although he noted that Digitalis had a remarkable "power over the motion of the heart," he apparently drew no inference of a connection between this fact and the diuresis which relieved so many, but not all, of his cases of dropsy.

We now believe that the diuresis is due entirely to improvement of the circulation, since no diuresis is observed after the administration of digitalis if the patient has no cardiac failure.

TABLE I

Dosage of various cardiac glycosides

	Av. quantity for full effect (Usually in divided doses)		Average daily dose for	Persistence of action
	Intravenous	Oral		
Digitoxin (Digitaline Nativelle)	1.2 mgm.	1.2 mgm.	0.2 mgm.	1-3 weeks
Digoxin	1.5 mgm.	2.0 mgm.	0.5 mgm.	4-7 days
Lanatoside C	1.5 mgm.	10.0 mgm.	1.5 mgm.	1-4 days
g Strophanthin (Ouabain)	0.5 mgm.	poorly absorbed		1-2 days

Fundamental actions

It is widely held to-day, in spite of some important dissenters, that the most important factor in the relief of congestive failure is an improvement in the contractions of the weakened cardiac muscle. The cardiac glycosides have been shown to affect the contractions of isolated cardiac muscles of all animals on which they have been tried, and not only of cardiac muscles but of most other muscles of the body. The effect depends upon the dose and the length of time the drug has acted. In rhythmically contracting heart, doses which will eventually poison the heart first, increase the speed and extent of contraction and relaxation. The maximum tension in systole is increased (2). At this stage the rate of the heart (frequency of beats) may or may not be changed. If it is changed, it is usually slower. As the action of the drug proceeds, the contractions become prolonged and relaxation is delayed and sluggish. In the frog heart the process continues with the frequency of the beat becoming slower and then with the development of irregularities till the heart stops in a partly or fully contracted state. Mammalian hearts do not stop in systole like the frog heart but this is probably due, not to a fundamental difference in reactions of the two kinds of cardiac muscle, but rather to the more complex organization of the mammalian heart. It would appear that the auricular tissues and conducting tissues are poisoned before the ventricular muscle. This so disorganizes the heart beat that the mammalian heart stops long before the ventricular muscle is ready to go into a state of systolic arrest.

Many workers have shown that if cardiac glycosides are applied to isolated hearts, or isolated strips of cardiac muscle, in about the concentration attained in patients receiving therapeutic doses, e.g. 1:40 million, striking increases in maximum tension are observed during contraction. It is significant, perhaps, that improved contractility is most evident when the isolated tissues have begun to weaken, as they always do fairly rapidly in their artificial environment (3).

Cardiac output

The effect of these glycosides on cardiac output has also been measured and it has been found consistently that in patients with cardiac failure and abnormally high pressures in the right auricle, the cardiac output per minute is increased,

often as much as 40 or 50 percent. At the same time the right auricular pressure is decreased, often by 10-15 cm. of water, which is a large relative change (4, 5).

In normal humans reports have been contradictory. Some observers (6) report no change or slight increases in cardiac output. Others have reported a definite decrease in cardiac output. All who have made measurements of the central venous pressure, however, agree that it is reduced even in normal subjects after therapeutic doses of various cardiac glycosides. A most striking series of observations to this effect was made recently by McMichael and Sharpey-Shafer (7) who injected doses of 1.5 mgm. of Digoxin intravenously into their patients and normal subjects. They used the technique of Cournand and Ranges (8) which involves passing a catheter into the right auricle from a vein in the arm. Through the catheter, measurements can be made of the right auricular pressure and samples of mixed venous blood can be withdrawn for the estimation of cardiac output by the Fick principle. These observers were so struck by the consistent reduction of venous pressure in all cases, although in their normal subjects the cardiac output was reduced, that they tried to explain all the beneficial effects of the Digoxin by some primary effect on venous pressure. They were not, however, able to suggest any way by which the drug might have directly affected the venous pressure. Till some such mechanism is demonstrated, and even perhaps not then, we need not abandon and disregard the vast body of evidence which supports the view that the cardiac glycosides act largely by improving the contractility of cardiac muscle. Nor need we believe that the contractility of normal heart muscle is impaired by therapeutic doses of cardiac glycosides. One important fact goes a long way towards explaining the anomalous reduction of cardiac output in the normal, if we accept the reality of that reduction. Therapeutic doses of several cardiac glycosides have been shown to decrease oxygen consumption of resting muscle, both when excised and when in the body. The reduction of total metabolism so produced amounts in the rat to about 13 percent (9). This, in itself, would represent a decrease of the same magnitude on the physiological demand of the heart. Still another explanation may be invoked. It has been known for a long time that cardiac glycosides cause a redistribution or reallocation of the circulating blood from the splanchnic region to more peripheral circuits, such as the skin (10), presumably by some constricting action on peripheral vessels which is more powerful in the splanchnic regions than in the periphery. By diverting the blood through longer circuits, return to the heart is delayed and venous pressure reduced. Cardiac output is thus reduced in accordance with Starling's Law, even though the cardiac muscle itself may be contracting more effectively.

The diuretic response

A definite diuretic response is most commonly observed when the drug acts rather quickly to remedy congestive failure with a good deal of œdema. The most important causes of increased urinary output are (1) decreased passive congestion of the kidneys when the venous pressure is reduced; (2) hydration of the blood as

fluid passes from the tissues to blood stream on the reduction of venous pressure. Another factor of possible importance, particularly in auricular fibrillation, is increased pulse pressure. Gesell (16) long ago demonstrated that pulsatile pressures are more effective in promoting renal filtration than an equivalent steady pressure.

Vagal effects

So called "vagal effects" of cardiac glycosides have received much attention and in this category have been lumped any observed slowing of the heart. The result has been confusing. We should, to begin with, exclude from the discussion any vagal effects that may be secondary to change in venous pressure. An increase in venous pressure causes an increase in heart rate by means of the well known Bainbridge reflex. One part of the mechanism involves inhibition of "vagus tone", i.e., decreases in the nervous impulses normally travelling down the vagus nerves to reduce the heart rate. Lowering the venous pressure would tend to increase vagal tone and decrease the heart rate. Having excluded this indirect "vagal effect", it is a real question whether there is any other. Normal humans, and patients with a regular and not too rapid heart rate, respond with only a small reduction in rate to therapeutic doses. With doses verging on the severely toxic, the rate may be very slow, due to heart block. With such doses the slowing is not abolished by atropine and may be attributed to a prolongation of the refractory period of the conducting tissues of the heart (11). This in turn may be regarded as an extension of the fundamental action of the drug on the contractile process in the heart, about which we can say little as yet.

The dramatic slowing of the heart seen in auricular fibrillation in which the heart rate is excessively rapid, does not necessarily require any other explanation than those given above, viz., indirect vagal action due to lowering of venous pressure, and in the later stages direct action of the drug on conducting systems of the heart.

The real argument about vagal effects turns about the slowing of the heart often produced in animals, particularly by impure preparations. These have been analysed by various kinds of cross circulation experiments and attributed either to excitation of the carotid sinus by the drug or to direct stimulation of vagal centres in the medulla. It begins to appear that these actions may be due to impurities or degradation products of the cardiac glycosides. Krayer (12) found in cross circulation experiments that pure Digitoxin had no stimulating action on the carotid sinus or on vagal centres in the medulla, whereas Digitoxigenin, a split product of Digitoxin, did have a powerful effect on the medullary centres, causing a dramatic slowing of the heart and in larger doses convulsions. Digitoxigenin, or other genins, may well be present in powdered leaf or impure extracts and serve to complicate the picture. In unpublished experiments in this laboratory we found that Strophanthin and Digoxin had no consistent slowing action, short of terminal poisoning. Lanatoside C, on the other hand, usually did slow the heart at an early

stage of its action. It seems, then, that "vagal effects", apart from indirect effects of decreased venous pressure, are not characteristic of cardiac glycosides as a class but may be a property of certain members of the group or of their degradation products.

The slowing of the heart, whether produced directly or indirectly by Digitalis, is probably important factor in the improvement of circulation, particularly in auricular fibrillation. A ventricle which beats very rapidly as well as irregularly, has insufficient time to recover its maximum contractility between beats. Many beats will accordingly be too feeble to produce an effective expulsion of blood. Insufficient time for adequate filling of the heart contributes further to inadequate stroke volume.

Nausea, vomiting and diarrhoea

Diarrhoea figures prominently in the account of Withering of the actions of Digitalis but with the smaller doses used nowadays it seems to have almost vanished as a troublesome side effect. Nausea and vomiting, however, still remain a nuisance and the search for the mechanism of their production has been prosecuted most energetically. The outcome has not been conclusive. For a while, due to the work of Hatcher et al (13), the fatalistic view prevailed that the emetic effects were a necessary consequence of the cardiac action, since it was demonstrated that the vomiting stemmed in some manner from reflexes from the heart on which Digitalis was working its effect. It is, however, easy to distinguish between emetic effects which appear after an oral dose, before any appreciable cardiac action is evident, and emetic effects which appear after full cardiac effects have been established. The latter may be due to reflexes from the heart or from central actions of the drug but at any rate they appear after absorption of the drug and hence may be called "systemic". The earlier type of nausea and vomiting is most likely due to local irritation of the digestive tract. The incidence of nausea and vomiting of the "local" type is much less with Digitoxin than with crude preparations of Digitalis. "Systemic" nausea and vomiting also are appreciably less frequent with Digitoxin (14).

Electrocardiographic changes

Toxic doses of cardiac glycosides can produce almost any kind of aberration in the electrocardiogram. Extra systoles (ectopic beats) are fairly common as early indicators of toxicity. Of greater interest are the changes to be seen after therapeutic doses (e.g., 6 Int. Units) in patients with a normal electrocardiogram. Some may show no change at all but most commonly changes are first noticeable in the R-T segment, particularly in leads 1 and 2. The T wave is often lowered or reversed or otherwise altered in shape. The duration of the Q-T interval is often shortened, indicating perhaps, a more rapid spread and retreat of the excitation wave over the ventricle. The change in the T wave has been made the basis of the first successful method of assaying the potency of Digitalis in the human(15). Suitable subjects with normal electrocardiograms must be chosen for this purpose. Definite changes in their electrocardiograms must be visible with variations in

dosage of not more than 22%. A single assay requires 6 or 8 such patients, each of whom is given 3 different doses of a standard preparation and one dose at least of the unknown. A month must elapse between each dose so that one assay requires four months or more to complete.

Assay problems

No reliable chemical method is available for the assay of the potency of crude preparations. They contain too many compounds closely allied chemically but differing in pharmacological effect. Bioassay methods based on the lethal dose for frogs or cats have been used for many years. The cat method gives results which are more consistent with the results on humans than does the frog method but even it may be unreliable at times. Such a statement can only be made with confidence, since a successful method of assay on humans has been developed. The cat method is now official in the United States and Canada for the assay of tinctures of Digitalis and powdered leaf. The small measure of uncertainty which will always remain regarding the potency of such preparations is not generally regarded as a serious handicap in their use. However, the fact that the uncertainty does exist, together with other considerations such as the decreasing cost of purified preparations, may well lead to their more general use in preference to the crude preparations.

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PULMONARY TUBERCULOSIS AND THE GENERAL PRACTITIONER

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Fifty years ago, when pulmonary tuberculosis was much more widespread than it is now, it was diagnosed and treated at home by the family physician. Tuberculosis sanatoria, and tuberculosis specialists, as we have them to-day, were virtually unknown. There were no X-rays and little bacteriological help, so diagnosis and treatment were empirical.

With the development of sanatoria, the introduction of X-ray diagnosis, and the increasing use of collapse therapy, the treatment of tuberculosis became a specialty, and the general practitioner was gradually relegated to a less and less important role.

As a result of this trend, and of the diminishing incidence of the disease, the general practitioner has little or no opportunity of keeping abreast of the advances in this field, and has little interest in it. This is very unfortunate, as the general practitioner should have a very important part to play in the modern campaign against tuberculosis.

I propose, therefore, briefly to survey the present methods of diagnosis, prevention, and treatment, with special reference to the role of the general practitioner.

Diagnosis

It is essential to have a controlling authority responsible for the overall supervision and co-ordination of the various diagnostic and treatment facilities. This is usually a function of the municipal health department, while the Provincial Department of Health exercises a general co-ordinating authority over the whole province. The diagnostic work falls into two main divisions:

1. *Clinics*

Chest clinics are operated by Sanatoria, general hospitals, and directly by the control authority, and deal principally with three classes of patient.

(a) Ex-patients. Since patients who have been under treatment for tuberculosis frequently relapse, it is very important that they should be re-examined at frequent intervals.

(b) Contacts. People who have been in close contact with known cases of tuberculosis have ten times as high an incidence of tuberculosis as the general population. When a new case is discovered, therefore, every effort is made to examine all the contacts, and they should be followed for five years at least.

(c) Suspects. These are patients who, because of suggestive symptoms, are referred by the family physician.

2. Surveys

It is well recognized that a person may have active tuberculosis without any symptoms, and, except for those in this group who may be contacts, they can only be discovered by surveys. Surveys are of two types.

(a) Group surveys. In these a section of the population is investigated which, because of some special factor, is considered likely to show a high incidence of tuberculosis. Contacts are such a group. We know the highest age incidence to be in adolescence and young adulthood, so high schools, universities, and young people's organizations are another such group. Nurses, because of occupation, and Indians, because of race, are other examples. These group surveys may be done by fluorography, or by tuberculin testing, with subsequent X-ray examination of positive reactors.

(b) Mass surveys. The development of the fluorograph permits the rapid X-raying of large numbers of people at very low cost so that the whole population can be covered. This has already been done in Saskatchewan, where about 90% of the population have been X-rayed at an average total cost of about 90 cents per capita. This method is highly effective, but depends on good organization and a high degree of public co-operation, which cannot usually be obtained without an extensive educational campaign. The ideal would be to carry this programme to the point where every one would be X-rayed every three to five years.

Treatment

Treatment of tuberculosis can be summed up in one word—rest. Rest must include physical rest, mental rest, and local rest of the diseased organ.

The principles of physical and mental rest require no elaboration. All I need say is that experience has shown that, with very rare exceptions, they cannot be adequately provided in the home; only in a sanatorium can tuberculosis be properly treated.

The use of surgical methods to provide rest for the lung has steadily increased and technique has steadily improved.

The commonest method has been intrapleural artificial pneumothorax. However, within the past few years, there has been a real change in our attitude towards this treatment. It is no longer considered a safe and simple procedure; but on the contrary is now regarded as a treatment fraught with very real dangers to the patient, and one which requires the greatest skill, judgment and attention. Many new contraindications have now been recognized. The new attitude toward pneumothorax may be briefly summed as follows:

(1) There are types of pulmonary tuberculosis which are not suitable for pneumothorax treatment in that they require permanent, rather than temporary collapse, for example, cavities, and fibro-caseous disease of the apices of some duration.

(2) If pneumothorax is established, it must be done with the proviso that it will immediately be abandoned if it is not satisfactory. Any of the following should be sufficient reason to abandon a pneumothorax.

(a) Inoperable adhesions

(b) Atelectasis

(c) Persistent effusion

(d) Persistent cavitation

(e) Evidence of visceral pleural thickening, etc.

In other words, unless the pneumothorax is perfectly satisfactory, it must be abandoned, for the end results of poor pneumothorax are often worse than those of the tuberculosis.

Extrapleural pneumothorax is now used only where intrapleural pneumothorax is impossible, and thoracoplasty is contraindicated. It is now realized that it is an irreversible procedure, and must be continued indefinitely with positive pressures, or replaced by thoracoplasty.

Phreniclasia has only very limited application. Its popularity has waxed and waned very greatly, but too often it has been done only for the sake of doing something. Its value is difficult to judge since much of its apparent benefit is probably due to bed rest.

Pneumoperitoneum (in conjunction with phreniclasia) is now an obsolete procedure.

Thoracoplasty is the major method of collapsing the tuberculous lung at present. The operative mortality has been greatly lowered now as a result of improved technique—chiefly the doing of the collapse by stages of two or three ribs at two to three weeks' interval. The wide applicability of this operation, not only as a primary elective collapse, but as a means of dealing both with tuberculosis and its complications, and with the problems arising from other forms of collapse, ensure its continued and increasing use.

Lobectomy and pneumonectomy are, for tuberculosis, a new approach and they are still in the process of development, and evaluation. Operative mortality is high but is being greatly lessened. Extirpation is at present done only in cases not suitable for thoracoplasty, such as basal and hilar cavities which do not collapse satisfactorily by any method, and the large caseous nodule, which will eventually excavate but cannot be collapsed until it does. The use of extirpation is limited by the restriction that the remaining lung must be healthy. It must be remembered that extirpation is only one part of the treatment of tuberculosis, and is *not* a curative procedure.

Chemotherapy has as yet no place in the treatment of tuberculosis. None of the agents yet developed has been shown to have any significant influence on the course of human tuberculosis. Undoubtedly, it is only a matter of time until an effective chemotherapeutic agent is discovered; but even then, the killing of the tubercle bacillus will leave a problem in the repair of the damaged lung.

I realize that this has been a very superficial and rapid glance over a large and complex field, but I hope it will be sufficient to give some idea of the achievements in this branch of medicine, and serve as background for my remarks on the role of the general practitioner.

First, it must be realized that this is pre-eminently a field of medicine which demands special training. It requires much practice to be able to interpret a chest X-ray, and a considerable amount of experience to plan a sourse of treatment for a tuberculous patient.

Assuming that the active treatment of tuberculosis is referred to the Sanatorium, there is still an important role for the family physician before and after the period of sanatorium trtaement.

Diagnosis still depends very largely on the family physician, for the majority of the patients are still diagnosed when they develop symptoms. In view of the tremendous importance of early diagnosis, a heavy responsibility rests on him.

I should point out now, that physical examination of the chest, even by an expert, is totally unreliable as a means of diagnosing or excluding tuberculosis. The physician who, after only a negative physical examination of the chest, decides that there is no tuberculosis, is living in a fool's paradise.

If for any reason the doctor suspects tuberculosis, the first step is a tuberculin test. The patch test is only about 80% as accurate as the intradermal so the latter is usually to be preferred. Careful attention to technique is very important. A negative test excludes tuberculosis, with rare exceptions; a positive test merely leaves the possibility. Ninety percent of positive reactors have no demonstrable evidence of tuberculosis, and another nine percent or better have only calcifications, without any active disease whatever. However when the patient has a positive reaction, he must be X-rayed. This can be done free or for, at the most, a nominal fee, at a chest clinic. Here the patient will undergo whatever investigation may be necessary to produce a diagnosis. These facilities are usually available within a reasonable distance, and the careful doctor will make good use of them. If they are not available, have a plate taken, but send it, *with a history*, to a sanatorium or radiologist for interpretation.

Generally speaking, most failures to diagnose tuberculosis are due to (a) failure to think of tuberculosis, (b) too great dependence on physical examination, (c) failure to make use of the available facilities for diagnostic consultation, (d) failure to realize that a couple of negative sputum examinations by no means rule out active tuberculosis.

So much for diagnosis. If the patient is found to require Sanatorium treatment, the family physician must see to it that the patient goes to Sanatorium. This requires a great deal of tact and sympathy, as there is still a great deal of ignorance and fear of tuberculosis and tuberculosis Sanatoria. The doctor can do a great deal to encourage the patient and his family and thereby facilitate the work of the Sanatorium. He can also do much harm by ill-advised pessimism, or by ill-advised optimism. He should not try to ease the shock by saying that the patient will be

in the Sanitorium only a few weeks, as this leads to a cruel disillusionment, which greatly upsets the patient. The usual minimum is six months, and the average about a year. The doctor should be perfectly frank, and answer all the questions honestly, without attempting to gloss over the unpleasant details at the expense of misinformation.

Next, the physician should make every effort to co-operate in getting the contacts examined, as this is a very important part of the preventive campaign.

When the patient is discharged from the Sanatorium the family physician is responsible for supervision of his regimen, and for the maintenance of his general health. He should be sure that the patient returns regularly for his review examinations at a chest clinic, as far too many ex-patients drop out of the sight of the Sanatorium once their treatment is complete.

The physician should not attempt to carry on pnuemothorax unless he has had thorough training, and is well aware of the recent advances.

May I now list briefly a few important points for the guidance of the general practitioner?

(1) Treatment of pulmonary tuberculosis has changed greatly in the past 15 years and is still improving rapidly.

(2) Tuberculosis can be treated only in a Sanatorium.

(3) It requires special training.

(4) Don't depend on your stethoscope to diagnose tuberculosis; as it is utterly unreliable.

(5) Use the diagnostic facilities available to you.

(6) Do tuberculin tests, and refer positive reactors for x-ray.

(7) Don't try to read X-rays of the chest unless you have had experience.

(8) If you send X-rays for interpretation, please send a history of the patient, as it helps a great deal.

(9) Most diagnoses of tuberculosis are missed because the doctor didn't think of it.

(10) Don't mislead the tuberculous patient. He must live with his tuberculosis, and can only do so if he understands his position.

(11) Co-operate with the Sanatorium with regard to contacts and review examinations.

(12) Visit your nearest Sanatorium occasionally and meet the staff who are treating your patients, and talk over their progress.

(13) Don't give pneumothorax treatments unless you're thoroughly well trained.

In general, therefore, the physician in general practice should not attempt to perform the functions of the Sanatorium or chest clinic, but rather act as their representative. In so doing, he greatly assists the specialist, and plays a very important part in the whole anti-tuberculosis campaign.

Abstracts

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MEDICINE I

STREPTOMYCIN IN THE TREATMENT OF SUBACUTE BACTERIAL ENDOCARDITIS. Priest, W. S. and McGee, C. J. JAMA Vol. 132 (3), Sept. 1946.

A CASE of S.B.E. in a boy of 8 years is described, in which penicillin alone was ineffective. Blood cultures revealed H. influenzae. With large doses of penicillin (500,000 to 1,000,000 units/day) and sulphamerazine to give 0.8 to 1.1 mgm/cc of blood, the patient was cured. The organism was sensitive to Streptomycin, in vitre.

Penicillin resistant strains of streptococci may be frequently encountered which are sensitive to Streptomycin. Three such cases are cited, one of which was an atypical Strep. viridans, the other two typical nonhaemolytic Streptococci. Their range of sensitivity to Streptomycin ranged from 0.1 to 1.0 unit/cc of blood. The drug produced sterilization of the valvular lesions in case 1, negative blood cultures in case 2 and cure in case 3. The dose of Streptomycin used was 50,000 units/day. In the three cases, serum levels of 3-12 units/cc of blood were obtained.

W. B. W.

MEDICINE II

ACUTE GENERALIZED MILIARY TUBERCULOSIS IN ADULTS. Chapman, C. B. and Wharton, C. M. New England Journal of Medicine, 235:8 (Aug. 22), 1946.

IN a review of 4066 cases autopsied at the Boston City Hospital between 1937 and 1941, 1.55 percent showed acute generalized miliary tuberculosis. The incidence of the condition among cases of tuberculosis of all types at autopsy for the same period was 20.3 percent.

Clinical diagnosis of the condition is difficult, since the most prominent symptoms recorded, viz., anorexia, weight loss, cough, night sweats, chest pain, and hemoptysis, may also occur in fibrocaseus pulmonary tuberculosis without miliary distribution.

Physical findings are seldom of much diagnostic assistance, the course of the temperature having no specific form, and the general appearance of the patient similar to that seen in any acute febrile illness. Rapid pulse rates were the rule, often out of all proportion to the degree of fever. At autopsy splenomegaly and hepatomegaly were found in less than 10 percent.

The only direct means of visualizing the miliary tubercles during life, i.e., by bone marrow autopsy and by ophthalmoscopic examination, were neglected in this series.

The average duration of the illness after the apparent acute onset was five and one half weeks.

Increased percentage of neutrophils and shift of the Arneth count to the left were present in 85% of the 35 cases in which differential counts were made. Leukopenia was frequent but not the rule.

Chronic tuberculous foci were found in 95%, involving the lungs, bowel, lymph nodes, and genito-urinary tract most frequently.

Miliary tubercles were found in the liver and spleen almost invariably, the bone marrow very frequently, and the kidneys and adrenals in about 50%. The importance of biopsy of the bone marrow and chest X-rays as diagnostic aids are emphasized. M. C. M.

MEDICINE III

Coronary Occlusion in Young Adults. By Maurice Newman. *The Lancet*, No. xii of Vol. ii.

The author of this article as principal medical officer in the British government had access to Service records and consequently undertakes to review fifty cases of coronary occlusion in adults under the age of thirty-five. This number of cases is small but certain features and conclusions of interest were noted.

(1) *Sex incidence* shows predominance in the male.

(2) *Body build.* The majority of cases were strikingly well developed and well nourished individuals with 43 of 50 cases weighing over 126 lbs. Earlier medical examination showed the individuals to be perfectly fit and free from all symptoms of heart trouble.

(3) *Previous infection* might have been of aetiological importance in only a few cases.

(4) *Physical strain* seemed to have no part in the predisposing causes since there was no evidence of such in 27 cases.

(5) *Preservice occupation*—Half of the subjects were doing heavy work before entry into the service. Consequently, it appears that a change from sedentary to manual occupation doesn't have any significance.

(6) *Prognosis* is much worse than in older age groups. Thirty-three cases of sudden death resulted out of 39 eventually fatal cases. Eleven are still living but all suffer from pain on exertion and breathlessness.

(7) *Autopsy*—Most amazingly, twenty-nine of the 39 cases undergoing autopsy showed no Thrombus. Thirty-seven showed the usual atheromatous changes met with in coronary disease of older people. In 17 cases, myocardial infarction of either recent or long standing was found.

In summary, the author stresses that coronary disease is not so rare as formerly thought in young adults and that degenerative changes of a remarkable degree can exist with no signs or symptoms. J. W. H.

MEDICINE IV

The Role of Emotions in the Production of Cardiovascular Changes. G. F. Strong. Can. Med. Assn. J. *55,* 344-348 (1946).

The simplest example of the role of the emotions in the production of cardiovascular disturbances is the palpitation and tachycardia produced by sudden fright. The effect of long continued fear, tension, or anxiety in the production of persistent cardiovascular symptoms is equally obvious and is the commonest cause of the symptom complex termed neurocirculatory asthenia, which may result in severe and persistent disability. Early diagnosis and adequate treatment can do much to prevent and relieve this common cardiac condition.

Neurocirculatory asthenia occurs in adults of both sexes. The ages most commonly affected are the same as for neuroses. The manifestations of the condition may be mild and transitory resulting from some obvious emotional strain or they may be severe and persistent. The commoner symptoms of this disorder: palpitation, extrasystoles, paroxysmal tachycardia, dyspnoea, cardiac pain, weakness or fatiguability, nervousness, insomnia, emotional instability, sensations of coldness in the extremities and vertigo, are discussed. Physical examination may reveal nothing but the evidences of the neurotic basis for this condition. History taking is important because it reveals the way in which the symptoms have developed and permits some insight into the patient as an individual. In differential diagnosis there are four conditions with which neurocirculatory asthenia is most apt to be confused: mild hyperthyroidism, early pulmonary tuberculosis, early mitral stenosis, and chronic brucellosis. The treatment of early and long established cases is discussed.

"The medical profession bears a grave obligation in this connection (diagnosis and treatment of neurocirculatory asthenia) because early diagnosis and adequate treatment will go a long way to prevent this disorder, whereas careless diagnosis or improper treatment may either produce the whole symtom complex or establish it so firmly as to increase the resulting disability."

G. W. B. C.

MEDICINE V

Streptomycin in the Treatment of Infections, a Report of One Thousand Cases. The Committee on Chemotherapeutics and Other Agents, National Research Council, C. S. Keefer, Chairman: J. Amer. Med. Assn. *132,* 4-11, 70-77 (1946).

"Streptomycin is a potent antibacterial agent that can be given intramuscularly or subcutaneously or injected directly into the subarachnoid space or the pleural or peritoneal cavity. Very little is absorbed from the gastrointestinal tract. The intramuscular route is the one of choice.

Following intramuscular injection, streptomycin is excreted in the urine and bile. It is necessary to maintain a concentration of the drug in the blood and tissues that is at least 4-8 times that required to inhibit the organisms in vitro. It is

necessary to repeat the injections every three to four hours. The dosage of streptomycin depends upon the type of infecting organism. . . . . One to four grams a day for 5 to 14 days may be required in certain acute infections.

In the treatment of empyema or meningitis it is advisable to use streptomycin topically by injecting it directly into the pleural cavity or the subarachnoid space.

Streptomycin has been most effective in the treatment of tularemia, Hemophilus influenzae infections, urinary tract infections due to gram-negative bacilli, bacteremias and meningitis due to gram-negative bacilli.

The results in typhoid, brucellosis and Salmonella infections have been disappointing and inconclusive.

The results in experimental and clinical peritonitis are sufficiently impressive to warrant a much more extensive clinical study. The same can be said for pulmonary infections due to Friedlander's bacillus and other gram-negative bacilli.

Further studies in Tuberculosis are urgently needed as soon as adequate supplies become available.

Untoward reactions are not infrequent and increase in frequency with increasing dosage. They consist of histamine-like reactions, headache, flushing of the skin, neurologic disturbances, vertigo, paresthesias, hypersensitive reactions, fever, skin eruptions and eosinophilia.

"The following conditions account for failure of streptomycin:

1. Treatment of infections that are not susceptible to the action of streptomycin; that is, the organism is so resistant that a concentration of streptomycin adequate to inhibit the growth of the organism cannot be maintained in the blood and tissues.
2. Inadequate dosage.
3. Development of resistance to streptomycin in vivo.
4. Change in the species of infecting organism during treatment.
5. Localization of infection in an area that cannot be reached by streptomycin."

G. W. B. C.

OBSTETRICS AND GYNECOLOGY I

ASPHYXIA OF THE NEW BORN. Russ, J. D. and Strong, R. A. American Journal of Obstetrics and Gynecology, 51:643 (May) 1946. (Abstracted from the International Medical Digest, 49:2 (Aug.) 1946.

THE writers, on the basis of over 1000 cases of resuscitation of the new born, reach the following conclusions:

(1) Asphyxia or apnea may be defined, clinically, as a lack of spontaneous effort to take a breath within 30 seconds after the cord is severed. If oxygenation of the blood stream does not occur within 1 or 2 minutes, there will be definite cerebral changes.

(2) The most frequent causes of asphyxia are
  (a) A prolonged or unduly traumatic delivery . . the greatest single cause.
  (b) Age of the mother: if over 35 years more likelihood of asphyxia. In general primipara produce more asphyxiated babies than do multipara.
  (c) Profound anemia of the mother may cause a cyanosis coming on in the child in 2-3 days.

(3) In the writer's experience the average Caesarian Section baby will not breathe spontaneously within 30 seconds, and intratracheal catheterization should be performed as a routine.

(4) The major principles in good resuscitation are
  (a) Minimum of handling
  (b) Immediate warmth
  (c) Clear open airway
  (d) Oxygenation of the blood stream within thirty seconds of severing the cord.

(5) The use of stimulating drugs is stated to be of little value in the resuscitation of the new born.

(6) The after care of the resuscitated new born is of equal importance to the resuscitation itself, and warmth, careful obsrvation, theuse of CO_2-oxygen mixture, and avoidance of feeding are emphasized.

A method of intratracheal resuscitation, and the rule of analgesic and anaesthetic agents in the production of neonatal asphyxia are described.

M. C. M.

PAEDIATRICS I

Immunization With Tetanus Toxoid: Persistence of Antitoxin and Effect of Stimulating Doses of Alum Precipatated Tetanus Toxoid After Five Year Period. A. McBryde and Mary A. Poston: J. Pediatrics *28*, 692 (1946).

The persistence of antitoxin after primary immunization, and the effects of stimulating doses at the end of one, two and one half, and five year periods are reported. A great increase in serum antitoxin titre was obtained after injecting 0.004 cc. of toxoid subcutaneously five years after the initial immunization. The authors conclude that this suggests that a stimulating dose is unnecessary although caution dictates its use.

The response in this series was rapid and adequate regardless of the level to which the antitoxin had fallen in the periods following primary immunization. Reactions were not severe and all school age children were able to continue in school. About 10% complained of soreness at the site of injection. An area of erythema was noted 24 hours after the subcutaneous injection and a small nodule formed which disappeared in about four weeks.

G. W. B. C.

DERMATOLOGY AND VENEREAL DISEASES I

RESULTS OF RAPID TREATMENT OF EARLY SYPHILIS. By J. R. Heller, Jr. J.A.M.A., Oct. 5, 1946.

A REPORT of length and great detail is presented by the chief of the venereal disease division of the U.S. public health service. Eleven methods of treatment including the use of penicillin, bismuth and arsenoxide in varying combinations and dosages are presented. Progress reports include a period of 12-15 months after active treatment of approximately 8000 patients.

Treatment begun in the primary stage gave much better results than that begun in the secondary stage or after relapse.

There was no significant difference in cases treated with penicillin alone or with penicillin plus arsenoxides.

Varying dosages of penicillin alone seemed to have no essentially different effect on results. The effectiveness of any penicillin treatment for early syphilis apparently is enhanced by the adjunctive use of bismuth.

Results from 40,000 units of penicillin every three hours for four days and 40,000 units every six hours for eight days showed no significant difference.

No deaths resulted from penicillin alone. When combined with adjunctive therapy a mortality rate of one in 4000 was noted.

In summary, the reviewer reaches various speculatory conclusions. These are:

Increased cure percentages were noticeable when a few doses of bismuth were added to the penicillin regimen. Apparently bismuth acts over a longer period, thus increasing the time over which a spirocheticidal agent is in continual action early in the disease.

There is a poor prognosis in relapsing syphilis. The differentiation between relapses and reinfection is most difficult. Relapses seem to develop from a failure of development of host resistance in rapid treatment, and should be treated by the more prolonged methods. J. W. H.

PUBLIC HEALTH I

IS AMOEBIASIS A MEDICAL PROBLEM IN CANADA? M. J. Miller: Can. Med. Assn. J. *55*, 336-340 (1946).

THE author concludes that amoebiasis is a medical problem in Canada, although not a major one. There will continue to be sporadic indigenous as well as imported cases of acute amoebiasis and while the number will not be large (there were only 162 cases reported for the period 1936-1945, with 14 deaths between 1940 and 1943), amoebic dysentery and more rarely amoebic hepatitis and liver abcess will occur and should be kept in mind in the differential diagnosis of such conditions.

A greater problem is presented by the relatively large (2% of the population, or about 240,000 in Canada) pool of chronic and carrier amoebiasis some of whom are undoubtedly showing symptoms of infection, the severity of which awaits further clinical investigation. The incidence of such cases is usually higher in troops returning from various subtropical theatres of war (11-13%) and inmates of

institutionalized groups such as orphanages and homes for the aged (20-37%).

A number of theories regarding the pathogenicity of *E. histolytica* are discussed and it seems probable that there is some extrinsic factor which is independent of the parasite or the host and which acts in some way to enhance the invasive power of the parasite and produces amoebic dysentery. The nature of this factor has not been established nor has it been determined whether it acts by breaking down the resistance of normal host mucosa or by stimulating the cytolytic powers of the parasite. G. W. B. C.

PUBLIC HEALTH II

THE DICK TEST IN MILITARY PERSONNEL. L. A. Rantz, P. J. Boisvert, and W. W. Spink: New Eng. J. Med. *235,* 39 (1946).

A POSITIVE Dick test is useful in indicating susceptibility to scarlet fever, that is, to the scarlatinogenic strain of hemolytic streptococci, but a negative reaction does not indicate immunity to infection by hemolytic streptococci.

27.8% of 1,280 men admitted to a military hospital with acute respiratory illnesses had a positive Dick reaction. Positive tests were less frequent in those cases (a) over the age of 20 years, (b) having more than twelve months military experience, and (c) whose premilitary residences had been in areas known to have low incidence of hemolytic streptococcal disease.

Exposure to the hemolytic streptococcus is considered essential for the establishment of a positive Dick reaction. This reaction is probably the result of acquired hypersensitivity to the products of the streptococcus rather than an indication of a natural susceptibility to a true toxin. G. W. B. C.

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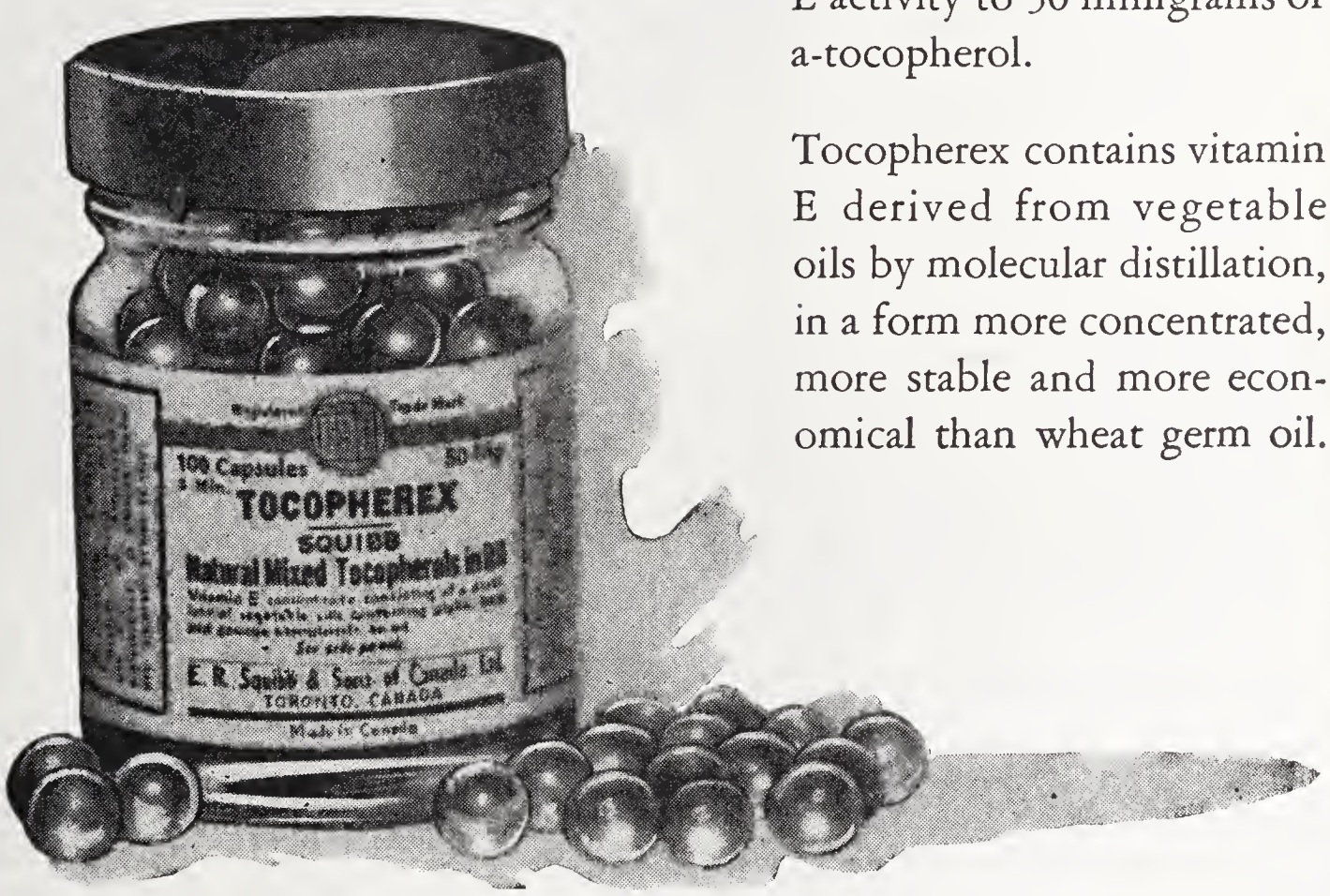

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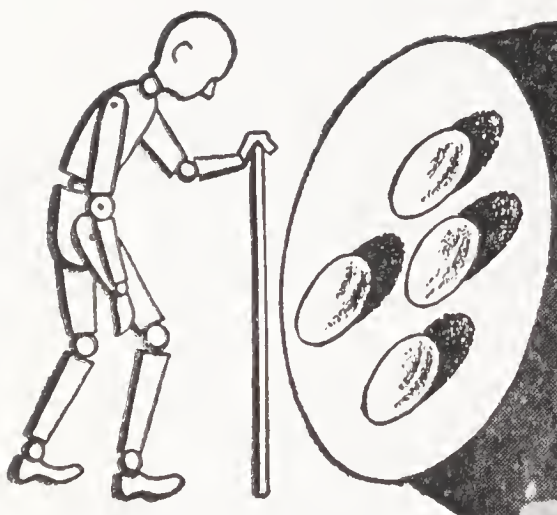

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